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VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/817,595	04/22/97	TURIANO A	MARGI-15

HM12/0104
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1642	20

DATE MAILED: 01/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/817,595	Turiano
Examiner	**Group Art Unit**
Geetha Bansal	1642

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on Oct 27, 99.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 10-24 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 10-24 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☑ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☑ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 1 sheet ☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other_____

Office Action Summary

DETAILED ACTION

Continued Prosecution Application

1. The request filed on October 27, 1999 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/817, 595 is acceptable and a CPA has been established. An action on the CPA follows.

2. An advisory action (Paper No: 17) was sent in response to the after final amendment received July 9, 1999. Applicant has not responded to the rejections of claims 10-24 in the advisory action.

3. Applicant's amendment filed July 9, 1999 (Paper No: 15/C) is acknowledged. Accordingly, claims 10-22, 24 have been amended.

Claims 10-24 are being examined.

Response to Arguments

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10-13, 17- 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims are ambiguous in that it is not clear from the claims whether the amounts of the MHC molecules in the two containers are effective separately or as a combined amount for the treatment of cancers. Clarification is requested.

B. Claims are indefinite in that the differences between the two sources of animal tissue , serum or cells in the two containers are not clear. Are the differences in the sources from different tissues or cells (e.g. muscle vs brain and T cells vs epithelial cells) or due to different batches of the same ? or different species or different members of the same species? or to different types of MHC molecules? Clarification is requested.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 17-22, 10-13, 14-16, 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims are drawn to a pharmaceutical composition useful for the treatment of cancer comprising MHC molecules, and methods of preparing the pharmaceutical composition, and a method of treating cancers. In determining the enablement of the instant claims, some of the factors that were considered were 1) nature of the invention, b) state of the prior art, c) level of predictability, d) amount of direction given, e) existence of working examples, f) quantity of experimentation to make the invention. The nature of the invention is such that the pharmaceutical composition of the instant claims must have a therapeutic benefit and b able to treat cancer. Treatment of cancer is recognized to mean treatment of the disease with its

accompanying symptoms and etiological development. The claims also are drawn to a composition comprising MHC molecules. The specification teaches the administration of MHC molecules to rats which have been inoculated with the AH-130 tumor cells, and estimating the number of tumor cells in the rats after the various administrations. There is no teaching in the specification that these data (drawn to the number of cells pre and post treatment) reflect the treatment of tumors. What is not clear is the survival of these rats past the treatment mode and the status of all symptoms associated with the cancer state. There are no working examples of an effective treatment of a cancer. There are a number of types of cancers that do not grow in the way exemplified - the exemplification is at best an alternate to an in vitro culture, as it serves to demonstrate a proliferation of tumor cells at a specific site (by virtue of the fact that they are specifically inoculated into the area as for e.g. into the lungs) with the therapeutic compositions also being administered into the same site. Secondly the window of testing for the efficacy of the composition is about 18 days and the time of administration begins as early as 4 days. This is very unlike the development of cancer in a human where it is not certain when the cancer state began or when tumor cells started forming. An effective therapeutic protocol for the treatment or prevention of the reformation of a tumor is subject to a number of factors which enter the picture beyond simply the administration of MHC molecules. The establishment and growth of a tumor is subject to variables beyond simply growing in an acceptable host. The specification does not indicate what type of cells the AH-130 cells are or whether the rats were immunosuppressed. The ability of a host to suppress and thereby prevent the tumor from establishing itself will vary depending upon factors such as the condition of the host, the type of tumor (rapidly proliferating or slowly proliferating) and the tumor burden. Moreover, the examples delineating the preparation of the compositions that are administered are extracts of the liver tissue from goat or calf. Firstly, the extract is a mixture of all molecules ranging in molecular weight from "10, 000-50, 000" (presumed to be Daltons). Such a mixture could have different proteins or chemically different molecules other than the MHC molecules, that could very well have therapeutic benefits.

Therefore, the claims are not enabled with respect to a pharmaceutical composition comprised of an effective amount of MHC molecules, because there is no guidance in the specification as to how to determine the amount of the MHC molecules in the extract. The facts of the experiments described are not sufficient to prove that the invention is enabled for treating cancers. Further, the disclosure does not provide working examples wherein all of the steps required to practice the method are employed. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art such as the treatment of cancer. In the instant case, the claims are so broadly drawn, the guidance is so limited, and the art is so unpredictable that skilled artisan is presented with a multitude of un-linked alternatives with no guidance as to which will enable use of the invention as claimed. Among these are (I) whether to use autologous or allogeneic MHC molecules (specification teaches xenogeneic "MHC molecules", (ii) which of many cancers to select for treatment, (iii) which of many antigens (e.g., endogenous/exogenous; cancer-associated/tumor-specific)are in the purified extract, (iv) which of many neoplastic diseases to select, and (v) what dosage, schedule, and route of administration will provide a successful therapeutic outcome.

Applicant's arguments have been considered but are not persuasive. Applicant does not address the issue presented in the previous office action sent 10/27/98 (specially on page 5) with respect to the working examples and the inclusion of other proteins in the MW range of 10,000 - 50, 000 as well as the presence of >50,000 MW proteins.

Secondly Applicant argues the relevance of the rat model has been questioned. It is stated that the rat model was not questioned, but rather as to whether the extrapolation of the studies conducted in the rat model of tumor growth to treatment of cancers with MHC molecules was rejected as being non-enabled as set out above.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Geetha P. Bansal whose telephone number is (703) 305-3955. The examiner can normally be reached on Mondays to Thursdays from 7:00am to 4:30pm and alternate Fridays from 7:00am to 3:30pm. A message may be left on the examiner's voice mail service.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Paula Hutzell, can be reached on (703) 308-4310.

11. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 29, 1999

GEETHA P. BANSAL
Pa. PATENT EXAMINER